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Antiviral Briefs

IMMUNE RECOVERY POSSIBLE IN CHILDREN

Researchers in Madrid have found that recovery of the immune system is possible in children with AIDS if they respond well to antiretroviral therapy. Taking 3 years, the study examined at 32 children with AIDS. The researchers also examined findings from 17 healthy children who were age-matched as controls. The children ranged in ages from 6 to 18 years of age in both groups.

Using three-color flow cytometry, the researchers looked at T-cell subsets and T-cell production by the thymus. The study found that 8 children were able to maintain their CD4 cell counts above 25% without the benefit of highly active antiretroviral therapy (HAART). They were identified as long-term asymptomatic individuals. Another 11 children were classified into AIDS clinical category C3 at the start of the study. After 3 years of receiving antiretroviral therapy, they were able to achieve CD4 cell counts greater than 500 cells/mm^3. The remaining 13 children remained in clinical category C3 throughout their follow-up period.

The 11 children who responded to HAART were discovered to have lymphoproliferative responses to mitogens and recall antigens. Such responses were similar to the 8 children who were considered long-term asymptomatic. The responsive group also had naive CD4 T subsets with similar percentages and absolute numbers as the long-term asymptomatic children and the control group. Compared to the 13 children who were nonresponsive, the therapy-responsive children had lower numbers of memory and activated T cells.

According to the researchers, HAART provides better control of HIV replication. Subsequently, this prevents naive T cells from turning into activated, memory, or effector CD4 cells. Another explanation may be naive-infected T cells being destroyed on a preferred basis. Atrophy of the thymus secondary to HIV infection may also explain the findings. The researchers concluded that T-cell restoration in the treatment-responsive children might result from the reconstituting of naive cells coming from the thymus combined with a decreased long-term activation of the child's immune system.

The complete study was published in *AIDS Res Hum Retroviruses* 2002;18:1395–1406.

FOUR-DRUG REGIMEN STUDIED

A French study has examined the efficacy of a four-drug regimen consisting of Combivir plus abacavir plus efavirenz in treatment-naïve patients. Study CNAF3008 evaluated the long-term safety, tolerance, and efficacy of a protease inhibitor (PI)-sparing regimen that was also easy to take and considered potent at reducing viral load to below the limits of detection. In this case, the regimen used consisted of three nucleoside reverse transciptase inhibitors (NRTIs) combined with one nonnucleoside reverse transcriptase inhibitor (NNRTI).

This was a small, pilot study consisting of 26 men and 5 women. Median baseline CD4 cell count was 322 cells/mm^3, while the median baseline viral load was 4.69 $\log_{10}$ copies per milliliter. The study lasted for 48 weeks. At the conclusion of 48 weeks, all of the participants were able to achieve a plasma HIV RNA level of less than 50 copies per milliliter. Specifically, the patients experienced a rapid and sharp decline in viral load. The median reduction was 2.7 $\log_{10}$ copies per milliliter. In some cases, this occurred as early as the fourth week of the study. Although 87% of the patients experienced one or more adverse event, none developed a hypersensitivity reaction to abacavir. The most common adverse events were gas-

trointestinal related, specifically nausea and vomiting.

The researchers did not find any statistically significant differences in triglyceride levels. However, participants did experience significantly increased levels of cholesterol and fasting glucose. Lipodystrophy was also not observed in the study participants. At the end of 48 weeks, the adherence level was 90%, with patients reporting they did not miss a dose or missed doses less than once a week during 4 previous weeks.

The complete study was published in *J Acquir Immune Defic Syndr* 2002;31:178–182.

WRONG INTERPRETATION OF MUTATIONS

According to a study from New York City, the majority of physicians and other providers are not getting their genotypic mutations and drug classes correct. In this study, only 25% were able to match most of the mutations to the affected drug classes.

The study consisted of a survey of 100 health care providers. Participants were nurse practitioners, physician's assistants, and physicians who were either in primary care or infectious disease. All of those surveyed used genotypic resistance testing on a regular basis. Each was asked on a questionnaire to correctly match 16 resistance mutations with 6 drug groups.

Survey results found that 36% of those participating were not able to match even one mutation with any of the drug groups. Out of the 100 providers surveyed, only 1 was able to correctly identify at least 1 mutation for each of the 6 drug groups. Among those who considered themselves "expert," 53% were able to identify mutations with at least 4 drug groups. The majority of respondents, 75%, said they used interpretations provided by the laboratories making the resistance tests as their source for guiding the test's interpretation. More than half, 58%, also used a fellow colleague as a guide source.

The researchers were surprised at the lack of basic mutation knowledge. In some cases, providers were not able to identify the M184V mutation for lamivudine and abacavir, and the K103N mutation for NNRTIs. They also cautioned providers not to rely solely on the interpretation provided by the laboratory. Instead, they should forge a relationship with an expert in genotype interpretation and seek out their advice when needed.

The complete study was published in *Clin Infect Dis* 2003;36:101–104.

STUDY SEEKS PARTICIPANTS

A study being conducted by the Whitman-Walker Clinic in Washington, D.C., is recruiting individuals who are either HIV-positive or HIV-negative. The study will observe the long-term effects of HIV infection and its various treatments. Those in the D.C. area will receive physical examinations, laboratory tests, and health assessments. In addition, those participating in the study will receive $25 for each study visit. Individuals who are interested can contact the Whitman-Walker Clinic at (202) 745-6172.

IL-2 THERAPY BENEFITS MAY BE LIMITED

A study from researchers in Cleveland, Ohio, suggests that interleukin-2 (IL-2) may have limited benefit in patients with HIV infection receiving antiretroviral therapy. Specifically, they found that IL-2 does not appear to provide enhancement of the patient's immunization response. It does, however, increase the patient's CD4 cell count.

The study recruited 38 patients who received either IL-2 along with their antiretroviral regimen or just HAART alone. They were treated for a minimum of 60 weeks before receiving a tetanus toxoid vaccine and immunization for hepatitis A and B. In addition to these three vaccines, the participants also got an inactivated glycoprotein 120-depleted HIV-1 vaccine.

When immunized, those participants who were in the IL-2 group had much higher CD4 cell counts compared to those individuals who

did not receive IL-2. The higher CD4 cell counts did not afford any advantage, however, as both groups demonstrated similar responses to their immunizations.

The complete study was published in *J Infect Dis* 2003;187:320–325.

NO DIFFERENCES IN HAART RESPONSE AMONG RACES

A study out of Denmark has concluded that all patients, regardless of their racial or ethnic backgrounds, benefit equally from antiretroviral therapy. The researchers looked at data from 389 white and 135 nonwhite patients with HIV infection residing in Denmark. They were followed 1 year after receiving their first antiretroviral regimen. At the conclusion of one year, the researchers did not find any differences in viral load between whites and nonwhites. The study did find, however, that nonwhite patients were more likely to delay the start of their therapy. In Denmark, which has a national health care system, access to healthcare and the cost of HAART are free to all.

The researchers believe studies from the United States showing differences among patients of different ethnic or racial backgrounds may stem from unequal access to healthcare and economic status. Factors that do appear to affect the use of antiretroviral therapy, according to the researchers, are HIV stigma, health beliefs, and language barriers.

The complete study was published in *Clin Infect Dis* 2002;35:1541–1548.

ADHERENCE LINKED TO BETTER QUALITY OF LIFE

French researchers have found that proper adherence levels lead to a normal quality of life in patients receiving antiretroviral therapy for 1 year. The study involved 654 patients who were enrolled in the APROCO cohort between 1997 and 1999. Researchers used the Medical Outcomes Study Short Form-36 (MOS SF-36) quality of life instrument, which was self-administered by the study participants.

Over the course of 12 months of treatment with antiretroviral therapy, 6 of the 8 scales showed significant improvement. In addition, the scale used to report body pain also had a significant decrease among patients who displayed good adherence to their regimens. At the end of one year, nearly 91% of the participants were still receiving a HAART regimen containing a protease inhibitor. According to the researchers, a plasma HIV-RNA level below the limits of detection was the most important predictor of a normal quality of life after 1 year.

Those participants with the best adherence levels were most likely to have a normal quality of life compared to participants who had less than optimal adherence records. Specifically, individuals who did not have any episodes of nonadherence during the 12 months were 63% more likely to have a normal quality of life than their nonadherent peers.

The complete study was published in *J Acquir Immun Defic Syndr* 2003;32:38–47.

HAART INCREASES THYMUS SIZE

Spanish researchers have discovered increases in the size of the thymus gland in adult patients receiving antiretroviral therapy. The study looked at thymus size in 21 patients 12 and 24 weeks after being placed on HAART. At the end of 24 weeks, the volume of the thymus gland was markedly improved. Along with an increase in size came greater production of naive T cells and elevated CD4 cell counts.

Previously, it was suggested that the thymus gland played an important in the repopulation of T cells after the administration of HAART in adult HIV-infected patients. Earlier studies had already demonstrated an increase in thymus size for pediatric patients after receiving HAART. According to the researchers, this new study suggests a functional role for the increased volume of the thymus in adult patients.

The complete study was published in *Clin Exp Immunol* 2002;130:121–126.

HCV TREATMENT MAY NOT BE SUITABLE

Another study has discovered that patients coinfected with HIV and hepatitis C virus (HCV) may not be suitable candidates to receive combination hepatitis C treatment with interferon and ribavirin. The Boston researchers found numerous social, behavioral, and medical barriers that preclude such patients from benefiting from the therapy.

The prospective study looked at 149 coinfected individuals. Those with HIV/HCV coinfection are most likely minority patients who live in large urban settings such as Boston. Only 44 (30%) of the patients evaluated in this study were considered eligible for treatment with interferon and ribavirin. Although they were eligible, only 16 of these patients actually ended up starting therapy.

Of the remaining patients, 23% were ineligible because of a lack of adherence with their regular medical visits. Active psychiatric disease disqualified 21% of those evaluated. Another problem was active drug or alcohol use during the previous 6 months, which was a reason in 23% of the cases. Decompensated liver disease accounted for 12%, while advanced HIV disease accounted for 13% of ineligibility. Medical comorbidities only accounted for 8% of disqualified patients.

The authors suggest that, in order to overcome these numerous barriers to treatment, specialized multidisciplinary teams are necessary which can provide earlier evaluation of these problem cases.

The complete study was published in *Clin Infect Dis* 2003;36:97–100.

DAILY PILL BURDEN AND ADHERENCE

A survey on adherence has identified a patient's total daily pill burden as the factor having the greatest impact on adherence. The survey, Perspectives on Adherence and Simplicity for HIV-Positive Patients on Antiretroviral Therapy (PASPORT) examined 299 patients. Most had been receiving antiretroviral therapy for a period of 4 years or more. The group was diverse in terms of gender, race, and ethnicity, and resided in the major metropolitan areas of Washington, Atlanta, New York, Miami, San Francisco, and Seattle.

Ten factors were evaluated. After pill burden, dosing frequency, adverse events, diet restrictions, pill size, and the number of refills were cited as having an impact on adherence. Other factors also identified as affecting adherence were number of insurance copays, number of prescriptions, number of medication bottles, and if bedtime dosing was required.

The study used a trade-off analysis, also called adaptive conjoint methodology. This allowed the researchers to look at the reality of patients making treatment decisions as they considered various trade-offs. Specifically, such trade-offs allowed the patients to tailor a specific regimen to fit their individualized lifestyle and preferences. The patients in the survey preferred two small pills taken at the same time each day with no food requirements or restrictions. Patients also wanted an acceptable side effect profile in addition to one monthly prescription and a single copay.

Dr. Valerie Stone from Massachusetts General Hospital presented the complete study at the annual meeting of the Infectious Disease Society of America.